

Atty Dkt. No.: STAN-213
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AMENDMENTS TO THE CLAIMS:

1. **(Previously Presented)** A method for identifying a ligand for a G protein-coupled receptor (GPCR), the method comprising:
 - contacting a G protein-coupled receptor (GPCR) with a candidate agent, the GPCR comprising a conformationally sensitive detectable probe positioned on or within a conformationally sensitive third intracellular domain of the GPCR with the proviso that no probe is positioned in a transmembrane domain; and
 - detecting a detectable signal of the conformationally sensitive detectable probe;
 - wherein detection of a change in the detectable signal in the presence of the candidate agent as compared to the absence of the candidate agent indicates the candidate agent is a ligand for the GPCR.
2. **(Currently Amended)** The method of claim 1, ~~wherein the conformationally sensitive intracellular domain is a third intracellular domain of the GPCR and~~ wherein the conformationally sensitive detectable probe is a detectable label attached to one or more amino acid residues within the third intracellular domain of the GPCR so that a conformational change in the GPCR in the presence of the candidate agent causes a change in the detectable signal of the detectable label.
3. **(Original)** The method of claim 2, wherein the detectable label is a fluorescent probe.
4. **(Original)** The method of claim 2, wherein the detectable label is attached to an amino acid residue corresponding to amino acid residue at position 265 in a β 2-adrenergic receptor.
5. **(Previously Presented)** The method of claim 1, wherein the conformationally sensitive detectable probe is a protease cleavage site within the GPCR so that a conformational change in the GPCR changes the accessibility of the protease cleavage site to protease cleavage, and the detectable signal is a protease cleavage product.
6. **(Original)** The method of claim 5, wherein the protease cleavage product is an N-terminal fragment of the GPCR.

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7. (Original) The method of claim 5, wherein the protease cleavage product is an C-terminal fragment of the GPCR.

8. (Currently Amended) The method of claim 5 ~~claim-4~~, wherein the detectable probe comprises two protease cleavage sites within the third intracellular domain of the GPCR, the cleavage sites flanking an epitope tag, wherein a conformational change due to the presence of the candidate agent agonist activity changes the accessibility of the protease cleavage site to protease cleavage, and the detectable signal is a polypeptide of the epitope tag released by protease cleavage of the two cleavage sites.

9. (Original) The method of claim 1, wherein the GPCR is immobilized by attachment to a support.

10. (Original) The method of claim 9, wherein the GPCR is attached to the support by binding of an N-terminal portion to the support.

11. (Original) The method of claim 9, wherein the GPCR is attached to the support by binding of an C-terminal portion to the support.

12. (Original) The method of claim 1, wherein the GPCR is in a membrane.

13. (Original) The method of claim 5, wherein the GPCR is expressed in a eukaryotic host cell.

14. – 19. (Canceled)

20. (Previously Presented) A method for identifying a ligand for a G protein-coupled receptor (GPCR), the method comprising:

contacting a plurality of G protein-coupled receptors (GPCRs) with a candidate agent, the GPCRs having a conformationally sensitive detectable probe positioned on or within a conformationally sensitive third intracellular domain, wherein the GPCRs are provided on an array at assigned coordinates; and

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detecting a detectable signal of the conformationally sensitive detectable probe;
wherein detection of a change in the detectable signal at a coordinate on the array in the presence of the candidate agent as compared to the absence of the candidate agent indicates the candidate agent is a ligand for the GPCR at the coordinate on the array.

21. (Previously Presented) The method of claim 20, wherein the detectable probe is a fluorescent probe.

22. (Previously Presented) The method of claim 20, wherein the GPCR is immobilized by attachment to a support.

23. (Previously Presented) The method of claim 20, wherein the GPCR is in a membrane.

24. (Previously Presented) The method of claim 20, wherein the detectable probe is a protease cleavage site.